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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
AEDER, SEAN E	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,784	MAHESWARAN ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Election filed 8/21/06 in response to the Office Action of 6/21/06 is acknowledged and has been entered. Applicant elected group I and breast tumor with traverse.

The traversal is on the ground(s) that a search and examination of all of the inventions would not impose a serious burden on the examiner. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the Office Action. As stated in the Office Action of 6/21/06, the inventions of group I represent distinct methods and the inventions of group II represent distinct products. Each group would require different searches in the literature, in part, due to the different classifications of each group. Searching the methods together with the products would be unduly burdensome because each search would require different searches in the literature that would not necessarily be co-extensive. Further, each group requires the consideration of different patentability issues. Furthermore, it is noted that the literature search, particularly relevant in this art, is not coextensive and is very important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Examiner has rejoined the following species of tumor: vulvar epidermoid carcinoma, cervical carcinoma, endometrial adenocarcinoma, ovarian adenocarcinoma, ocular melanoma, prostate tumor, breast tumor, cutaneous tumor, and germ cell tumor.

Claims 1-35 are pending.

Claim 35 is withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 1-34 are currently under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-34 are rejected as vague and indefinite for reciting the terms "MIS" and "rhMIS" as the sole means of identifying polypeptides of the claimed methods. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. Amending the claims to specifically and uniquely identify MIS and rhMIS by SEQ ID NOs can obviate the rejection.

Claims 1-34 are rejected because independent claims 1 and 18 recite methods that result in "decreased side-effects". It is unclear to what said side-effects are decreased.

Claims 9 and 26 are rejected as indefinite for reciting: "substantially free of N-terminal fragment". It is not clear from the claims or the specification what is meant by "substantially". This renders the claims indefinite because the term "substantially" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Given the above reasons, the metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-16 and 18-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Donahoe et al (US Patent 5,661,126; 8/26/97).

Claim 1 is drawn to a method comprising administering to a patient in need thereof MIS and interferon, that results in decreased side-effects, thereby increasing

anti-tumor effect of interferon. Claim 2 is drawn to the method of claim 1 wherein said breast cancer patient has primary tumor growth. Claim 3 is drawn to the method of claim 1, wherein said patient has metastatic growth. Claim 4 is drawn to the method of claim 1, wherein said patient has a tumor selected from the group consisting of vulvar epidermoid carcinoma, cervical carcinoma, endometrial adenocarcinoma, ovarian adenocarcinoma, ocular melanoma. Claim 5 is drawn to the method of claim 1, wherein said patient has a tumor selected from the group consisting of prostate tumor, breast tumor, cutaneous tumor, and germ cell tumor. Claim 6 is drawn to the method of claim 1, wherein MIS has a molecular weight of 140 kDa or 70 kDa. Claim 7 is drawn to the method of claim 6, wherein said MIS is proteolytically cleaved by reacting with a proteolytic compound to form protein fragments having a molecular weight of about 57 kDa and 12.5 kDa. Claim 8 is drawn to the method of claim 1, wherein MIS is rhMIS. Claim 9 is drawn to the method of claim 1, wherein said MIS is C-terminal fragment of MIS substantially free of N-terminal fragment. Claim 10 is drawn to the method of claim 9, wherein said C-terminal fragment of MIS has a molecular weight of about 25 kDa or about 12.5 kDa. Claim 11 is drawn to the method of claim 10, wherein the C-terminal fragment of MIS is derived from rhMIS. Claim 12 is drawn to the method of claim 1, wherein said interferon is selected from the group consisting of interferon-α, interferon-β, interferon-ω, interferon-τ, and interferon-γ. Claim 13 is drawn to the method of claim 12, wherein said interferon is interferon-γ. Claims 14-16 are drawn to the method of claim 1, wherein said interferon is administered in an amount of about 10 international units per administration to an amount of about 100,000 international units per

administration. Claim 18 is drawn to a method comprising administering to a patient an effective amount of MIS and an effective amount of interferon that results in decreased side-effects. Claim 19 is drawn to the method of claim 18, wherein said patient has primary tumor growth. Claim 20 is drawn to the method of claim 18, wherein said patient has metastatic tumor growth. Claim 21 is drawn to the method of claim 18, wherein said patient has a tumor selected from the group consisting of vulvar epidermoid carcinoma, cervical carcinoma, endometrial adenocarcinoma, ovarian adenocarcinoma, ocular melanoma. Claim 22 is drawn to the method of claim 18, wherein said patient has a tumor selected from the group of prostate tumor, breast tumor, cutaneous tumor, and germ cell tumor. Claim 23 is drawn to the method of claim 18, wherein said MIS has a molecular weight of 140 kDa or 70 kDa. Claim 24 is drawn to the method of claim 23, wherein said MIS is proteolytically cleaved by reacting with a proteolytic compound to form protein fragments having a molecular weights of about 57 kDa and 12.5 kDa. Claim 25 is drawn to the method of claim 18, wherein said MIS is rhMIS. Claim 26 is drawn to the method of claim 18, wherein said MIS is C-terminal fragment of MIS substantially free of N-terminal fragment. Claim 27 is drawn to the method of claim 26, wherein said C-terminal fragment of MIS has a molecular weights of about 25 kDa or about 12.5 kDa. Claim 28 is drawn to the method of claim 27, wherein the C-terminal fragment of MIS is derived from rhMIS. Claim 29 is drawn to the method of claim 18, wherein said interferon is selected from the group consisting of interferon-α, interferon-β, interferon-ω, interferon-τ, and interferon-γ. Claim 30 is drawn to the method of claim 18, wherein said interferon is interferon-γ. Claims 31-33 are

drawn to the method of claim 18, wherein said interferon is administered in an amount of about 10 international units per administration to an amount of about 100,000 international units per administration.

Donahoe et al teaches a method comprising administering MIS and interferon to a patient having has a tumor selected from the group consisting of vulvar epidermoid carcinoma, cervical carcinoma, endometrial adenocarcinoma, ovarian adenocarcinoma, ocular melanoma, prostate tumor, breast tumor, cutaneous tumor, or germ cell tumor (see column 1 lines 24-27, column 15 lines 43-50, and column 21 lines 25-38, in particular). It appears the claimed method is the same as the method taught by Donahoe et al, therefore the method taught by Donahoe et al would result in decreased side-effects, thereby increasing anti-tumor effect of interferon. Donahoe et al further teaches said method wherein said patient has primary tumor growth or metastatic tumor growth (see column 15 lines 47-50, in particular). Donahoe et al further teaches a method wherein MIS has a molecular weight of 140 kDa or 70 kDa (see column 1 lines 44-49, in particular). Donahoe et al further teaches a method wherein said MIS is proteolytically cleaved by reacting with a proteolytic compound to form protein fragments having a molecular weight of about 57 kDa and 12.5 kDa (see column 1 lines 49-54, in particular). Donahoe et al further teaches a method wherein MIS is rhMIS (see Example 3, in particular). Donahoe et al further teaches a method wherein said MIS is C-terminal fragment of MIS substantially free of N-terminal fragment (see column 2 lines 39-54, in particular). Donahoe et al further teaches a method wherein said C-terminal fragment of MIS has a molecular weight of about 25 kDa or about 12.5 kDa 9

(see column 2 lines 39-42, in particular). Donahoe et al further teaches a method wherein the C-terminal fragment of MIS is derived from rhMIS (see Example 3, in particular). Donahoe et al further teaches a method wherein interferon is selected from the group consisting of interferon-α, interferon-β, interferon-ω, interferon-τ, and interferon-γ (see column 21 lines 26-40 and column 26 lines 34-36, in particular). Donahoe et al further teaches a method wherein said interferon is interferon-γ (see column 26 lines 34-36, in particular). Donahoe et al further teaches a method wherein interferon would be effective between about 0.001 and 10.0 mg/kg body weight of a patient, which is an amount of about 10 international units per administration to an amount of about 100,000 international units per administration (see column 21 lines 16-20, in particular).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donahoe et al (US Patent 5,661,126; 8/26/97) in view of Cohen (Int. J. Radiation Oncology Biol. Phys., 2/87, 13(2): 251-258).

Claims 1-16 and 18-33 are described above. Claim 17 is drawn to the method of claim 1, wherein said interferon is administered in an amount less than 1×10^6 International Units per administration. Claim 34 is drawn to the method of claim 18, wherein said interferon is administered in an amount less than 1×10^6 International Units per administration.

The teachings of Donahoe et al are described above. Donahoe et al further teaches that that a chemotherapeutic agent, such as interferon, which is combined with MIS will have an additive effect on the treatment of tumor (paragraph bridging columns 20-21). Donahoe et al further teaches that the quantity of chemotherapeutic agent, such as interferon, used in treating the tumors of this invention can be reduced from the manufacturer's recommended dose, thereby reducing undesirable side-effects (see paragraph bridging columns 20-12).

Cohen teaches that in successful cancer therapy, the tumor must be eradicated without significant damage to adjacent tissues or organs (page 251). Cohen teaches a method of optimizing dosages of compounds used to treat tumors (page 251, in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer MIS and interferon to a cancer patient as taught by Donahoe et al and optimize the amounts of MIS and interferon in said administration as taught by Cohen. Further, one would have been motivated to administer interferon at doses below 1 x 10^6 International Units per administration since Donohue et al indicates that a low dose of interferon, in combination with MIS administration, would predictably treat tumors. Further, one of skill in the art would have a reasonable expectation of success in performing the claimed methods since administration of MIS and interferon is well known and conventional in the art.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER